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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/921,512	08/01/2001	Mattias Luukkonen	PRI-0019 (ORT-1461)	6102

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EXAMINER	
SMITH, CAROLYN L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 06/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/921,512	LUUKKONEN ET AL.	
	Examiner	Art Unit	
	Carolyn L Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *2-9 and 12-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 10, 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-24* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03252004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments and remarks, filed 4/9/04, are acknowledged. Amended claims 1, 10, and 11 are acknowledged.

Applicant's arguments, filed 4/9/04, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The present title is directed to gene expression profile for KSHV infection and methods for treating the same, whereas in contrast the elected claims are specifically directed to a method for inhibiting replication of KSHV by inhibiting c-Kit signaling pathway.

Claims 1, 10, and 11 are herein under examination.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
It does not identify the citizenship of the inventor on page 7. It states the "Country of Citizenship" is "German", which is not a country.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

NEW MATTER

Claims 10-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Sections of the specification cited by Applicants do not appear to provide written support for a "first" and "second" compound, as stated in instant claim 10. Because the introduction of these terms lacks adequate written support, the terms "first" and "second", as filed 4/9/04, are considered NEW MATTER. Claim 11 is also rejected due to its dependency from claim 10. This rejection is necessitated by amendment.

Claim Rejections – 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The

factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of the skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

LACK OF SCOPE OF ENABLEMENT

The rejection of claims 1 and 10 is maintained under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain compounds to inhibit or otherwise modulate KSHV replication, does not reasonably provide enablement for all compounds.

This rejection is reiterated and maintained for reasons of record.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification does provide enablement for using several compounds in the method that were laboratory-tested, such as 2-phenylaminopyrimidine derivate STI 571, PDTC (pyrrolidinedithiocarbamate), trans-retinoic acid, SB203580, calcitonin gene-related peptide (CGRP), and CGRP-8-37 peptide, InCELLect AKAP St-Ht31, and St-Ht31-control peptide, haloperidol, phorbol-112-myristate-13-acetate (PMA), Ganciclovir, 15-deoxy$^{(12-14)}$ prostaglandin J2 (page 44 of specification), but does not provide reasonable enablement for the broad term "compound" as stated in claims 1 and 10. There are millions of compounds that scientists have discovered, and it would require undue experimentation to determine which

compounds are effective in the claimed method. A narrower group of compounds would be required to resolve this undue experimentation issue. Also, due to the unpredictability of finding effective compounds that inhibit replication of KSHV, one skilled in the art would not be able to reasonably test any compound available to make and use the invention in a reasonable amount of time. Therefore, the above-mentioned lack of scope of enablement rejection is set forth.

Applicants state one skilled in the art would be able to practice Applicants' claimed invention without being required to perform undue experimentation due to the direction and working examples provided by Applicants. Applicants then state particular instances in the specification that provide such examples. While these examples do enable one to make and use the several compounds listed above, undue experimentation would be required to test compounds in general, without an adequate narrowing down of the potential compounds to be used. Finding effective drugs is an unpredictable art, as stated by Stoughton et al. (P/N 5,965,352) as even an "ideal drug", which affects only a single constituent in a cell without direct effects to other constituents, will have complicated and often unpredictable indirect effects (col. 9, lines 34-55). Stoughton et al. state drug screening involves testing numerous compounds via high-throughput assays providing little or no information about the effects of a compound at the cellular or organismal level which must be determined via further testing (col. 1, lines 46-67). Such additional testing beyond high-throughput assays with unpredictable results demonstrates undue burden if the compounds are not limited in number. Therefore, this lack of scope of enablement rejection is maintained.

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The rejection of claims 1, 10, and 11 is necessitated by amendment under 35 U.S.C. 102(e)(2) as being anticipated by Capon et al. (P/N 6,103,521).

One reasonably broad interpretation of claim 1 is that there is no direct inhibition required of the c-Kit signaling pathway. Capon et al. disclose using multispecific chimeric receptors containing multispecific extracellular inducer-responsive clustering domain to recognize antigens or epitopes from a single pathogen to treat Kaposi's sarcoma-associated herpes virus (KSHV) (col. 16, lines 58-67). Capon et al. disclose using proliferation signaling domains from tyrosine kinase growth factor receptors, including c-Kit. Although the site of action is not defined in the treatment stated by Capon et al., one reasonable interpretation of treatment to a viral infection is that it would essentially stop all viral activities, including its replication, as stated in claim 1. Capon et al. disclose administering a dose of taxol to a patient (col. 17, lines 57-65). Capon et al. cite a reference of Sorrentino et al. (1992, Science Vol. 257, pages 99-103). The Sorrentino et al. reference is not being used as a prior art reference but merely to expand on a point made by the Capon et al. reference. Sorrentino et al. describe a dosage of taxol in Figure 2A as 10mg/kg and 8.5 mg/kg which clearly represents the presence of

more than one compound of taxol. As the first and second compounds in claims 10 and 11 can be reasonably interpreted to mean two compounds that are not necessarily different compounds and the compound taxol stated to meet at least the second compound requirements (instant claim 11), Capon et al. anticipate the method of administering taxol. Capon et al. disclose titrating therapeutic agents to obtain maximum therapeutic benefit (col. 17, lines 65-67) which represents administering a therapeutically effective amount of a drug. Capon et al. disclose the application of combination therapies for treatments of herpes virus infections although side-effects may occur (col. 1, lines 58-64). Thus, Capon et al. anticipate the limitations of claims 1, 10, and 11.

This rejection is necessitated by amendment.

Applicants state that contrary to the assertion by the Office, the method of claim 1 includes a step of administration of a therapeutically effective amount of a compound that inhibits replication of KSHV and c-Kit signaling pathway. This statement regarding the inclusion steps of the method is acknowledged; however, the Office's assertion that no direct inhibition is required of the c-Kit signaling pathway is maintained as the claim fails to explicitly state that the inhibition is direct. Applicants state that the Capon et al. reference does not teach or disclose such a method. This statement is found unpersuasive as the Capon et al. reference discloses such limitations as described above. Applicants statement is an assertion without support and have failed to provide substantive reasoning as to why the above-mentioned prior art rejection would be considered invalid. Applicants state that claims 10 and 11 are directed to administering a first compound that inhibits receptor tyrosine kinase c-Kit and a second compound that modulates KSHV replication by a mechanism other than inhibition of receptor tyrosine kinase c-Kit. Applicants further state that the Capon et al. reference does not mention

administering a therapeutically effective amount of a first and second compound. It is noted that the claims make no mention that these two compounds are different from each other, such that a dosage (which normally contains more than a single compound of a particular drug) meets the requirements of administering a first and second compound. Applicants state that the Capon et al. reference does not teach an additional method step comprising administering a therapeutically effective amount of a first compound that inhibits receptor tyrosine kinase c-Kit. This is found unpersuasive as the treatment to a viral infection is that it would essentially stop all viral activities, including replication, as further described in the rejection above. Because Applicants failed to provide reasoning or support as to why such an interpretation would be considered invalid, the rejection is considered proper.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

June 14, 2004

Ardin H. Marschel 6/23/04
ARDIN H. MARSCHEL
PRIMARY EXAMINER